Divergent RNA-Binding Proteins, DAZL and VASA, Induce Meiotic Progression in Human Germ Cells Derived In vitro.

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Public Summary:
This manuscript reports the use of divergent internal factors, that regulate RNA metabolism, to promote the development of germ line cells from induced pluripotent stem cells and human embryonic stem cells. This study suggests that the induced pluripotent stem cell and human embryonic stem cell systems can be used to probe fundamental aspects of human germ line development, aspects that are likely to be implicated in important developmental processes and pathologies such as birth defects associated with chromosome errors.

Scientific Abstract:
Our understanding of human germ cell development is limited in large part due to inaccessibility of early human development to molecular genetic analysis. Pluripotent human embryonic stem cells (hESCs) and induced pluripotent stem cells (iPSCs) have been shown to differentiate to cells of all three embryonic germ layers, as well as germ cells in vitro, and thus may provide a model for the study of the genetics and epigenetics of human germ line. Here, we examined whether intrinsic germ cell translational, rather than transcriptional, factors might drive germ line formation and/or differentiation from human pluripotent stem cells in vitro. We observed that, with overexpression of VASA (DDX4) and/or DAZL (Deleted in AZoospermia Like), both hESCs and iPSCs differentiated to primordial germ cells (PGCs) and maturation and progression through meiosis was enhanced. These results demonstrate that evolutionary-unrelated and divergent RNA-binding proteins can promote meiotic progression of human derived germ cells in vitro. These studies describe an in vitro model for exploring specifics of human meiosis, a process that is remarkably susceptible to errors that lead to different infertility related diseases.